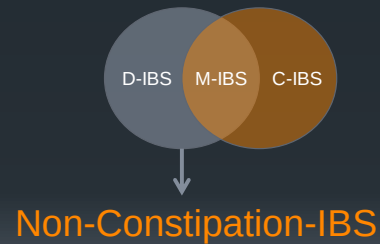
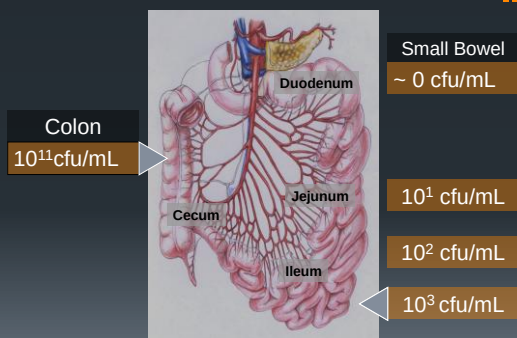


Small intestinal bacteria

Mark Pimentel, MD
Director, GI Motility Program
Cedars-Sinai Medical Center



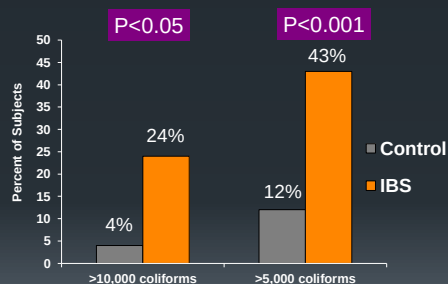
SIBO- What is it?



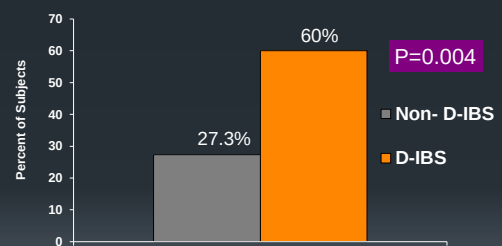
Breath Testing is abnormal in IBS



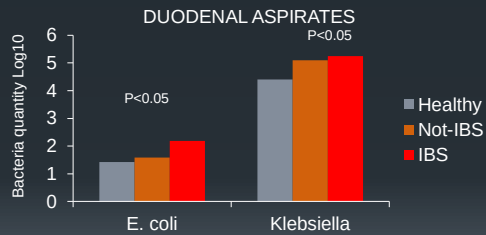
Small Bowel Culture in IBS



SIBO and IBS



Single Organism PCR in IBS

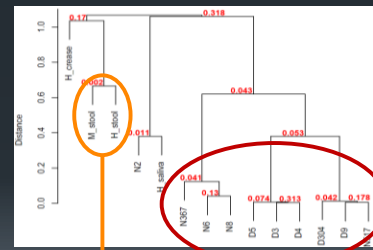


N=77 non-D-IBS, N=35 D-IBS

Pyleris, et al. UEGW, 2012

Stool vs. Small bowel

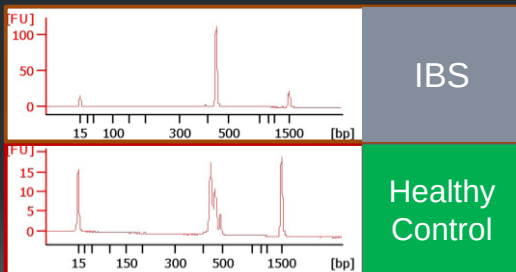
-Dendrogram with hierarchical clustering



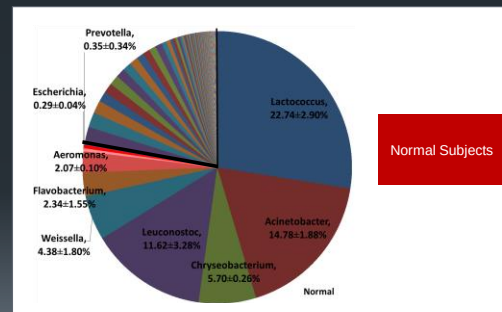
Human stool flora are more closely related to mouse stool than to human small intestine.

Human
Small Bowel
Flora

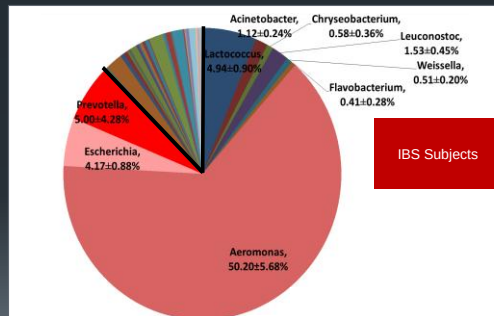
Agilent Plots of Normal and IBS



Sequencing Results- Normal small bowel



Sequencing Results- IBS small bowel



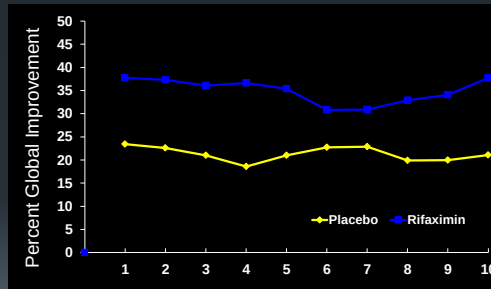
Species Differentiation in IBS vs Controls

Level	Organism	P-value
Elevated in IBS	Aeromonas spp.	0.0046
	Eschericia spp.	0.022
Reduced in IBS	Chryseobacterium	0.003
	Lactococcus spp	0.032
	Acinetobacter spp	0.034

Issues in the Study of Small bowel flora

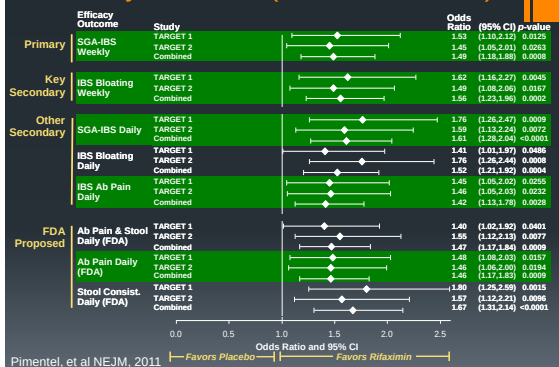
Challenges	Benefits
-Controls often have no bacteria	-Study of viable organisms
-Small quantities of DNA to work with	-Small bowel more biologically important
-Acquiring samples requires invasive approach	-Lower number of species which is simpler to deal with

Rifaximin: First Controlled Trial

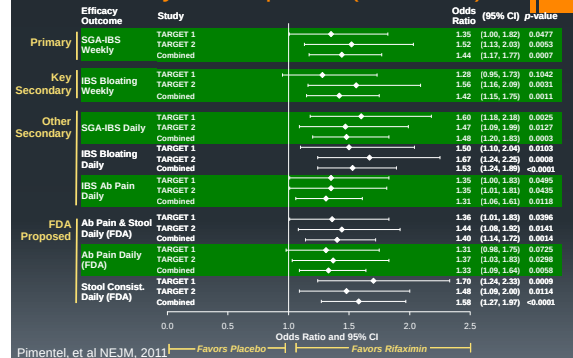


Pimentel, et al, Ann Intern Med, 2006

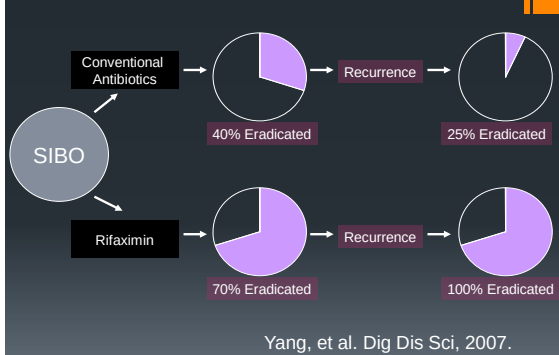
Primary Outcome (4 weeks after Tx)



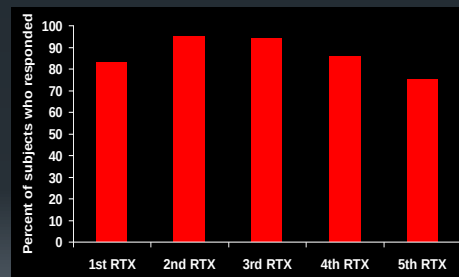
Durability of Response (3 months)



Antibiotic Resistance

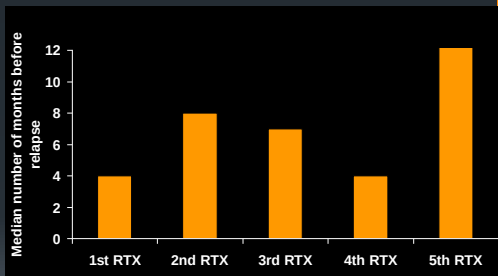


Retreatment with Rifaximin



Pimentel, et al. Dig Dis Sci, 2011.

Retreatment with Rifaximin



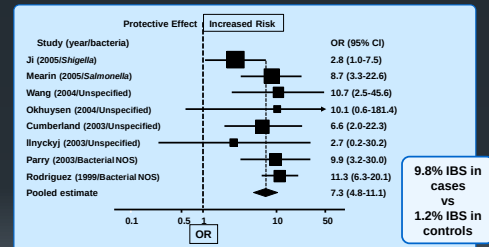
Note: RTX is the retreatment number. In this figure, the time (in months) refers to the number of months of wellness before the treatment number in each column. For example, for 1 RTX, it would be the number of months the patient was well after the first rifaximin administration and prior to the 1 RTX.

Note: Rare patients were missing accurate dates and thus were not included here.

Note: The median is a more accurate depiction of the duration of benefit since the ranges were wide.

Pimentel, et al. Dig Dis Sci, 2011.

Risk of PI-IBS Increases 7-fold After Infectious Gastroenteritis*

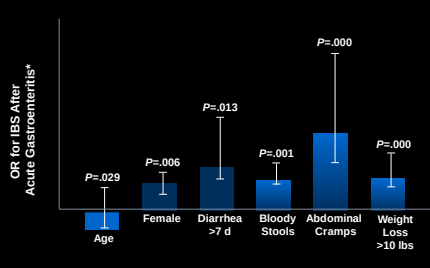


9.8% IBS in cases
vs
1.2% IBS in controls

*Systematic review of 8 studies involving 588,061 subjects; follow-up ranged from 3 to 12 months.

Halvorsen HA et al. Am J Gastroenterol. 2006;101:1894-1899.

Characteristics of Acute Illness Identify Patients at Risk for PI-IBS



*Identified from multiple logistic regression analysis from 2669 participating in the Walkerton Health Study. Marshall JK et al. Gastroenterology. 2006;131:445-450.

Salmonella and PI-IBS

	Percent with IBS at 1 year	Relative Risk (CI)
Irritable Bowel	12%	5.2 (2.7-9.8)
Non-ulcer dyspepsia	15%	7.8 (3.1-19.7)

Nausea was a risk factor for NUD

Mearin, et al. Gastro, 2006

NORMAL

ACUTE GASTROENTERITIS

90%

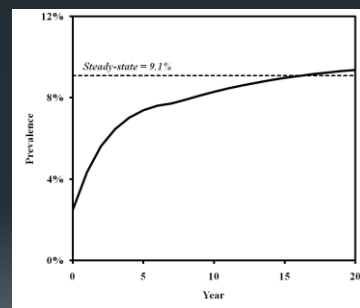
COMPLETE RECOVERY

10%

~GENETIC SUSCEPTIBILITY
~ABNORMAL HOST RESPONSE
~TOXIN INTENSITY

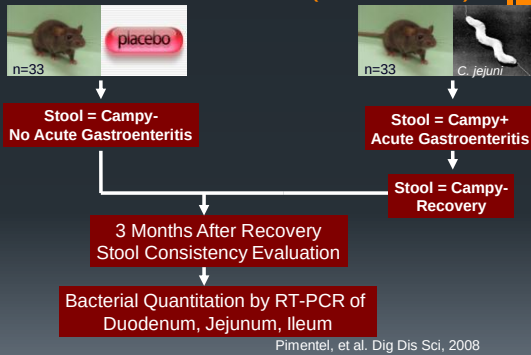
FUNCTIONAL GI DISEASES?

Post-infectious IBS = IBS

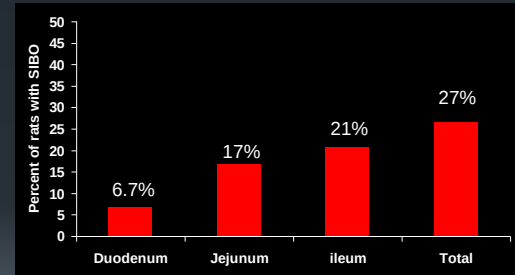


Shah, et al J Neurogastroenterol Motil, 2012

Mechanism: Rat Model (SIBO = IBS)



Mechanism: Rat Model (SIBO = IBS)

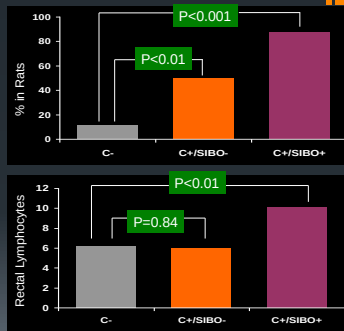


3 months after *Campylobacter jejuni* 81-176 infection

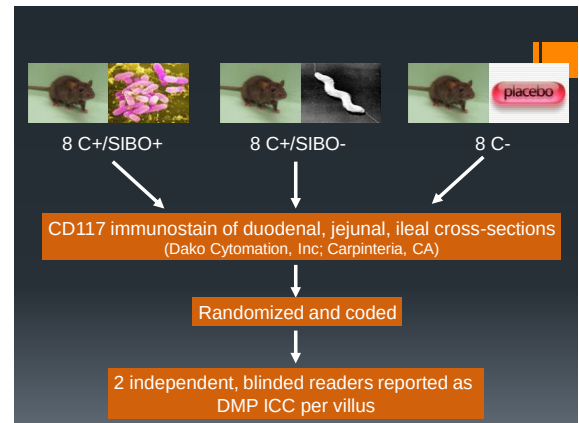
Pimentel, et al., Dig Dis Sci, 2008

Mechanism: Rat Model (SIBO = IBS)

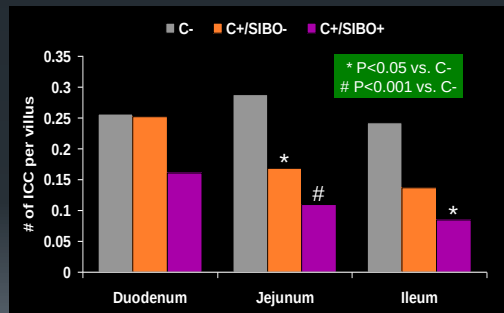
Persistent altered stool consistency



Pimentel, et al. Dig Dis Sci, 2008

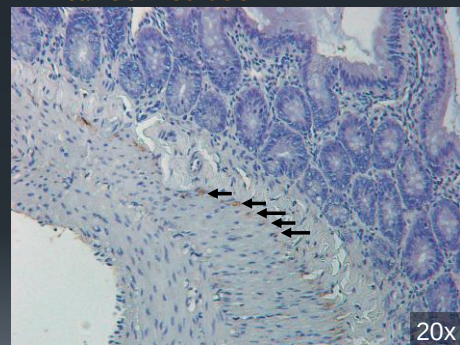


Reduction in ICC: Lowest in SIBO



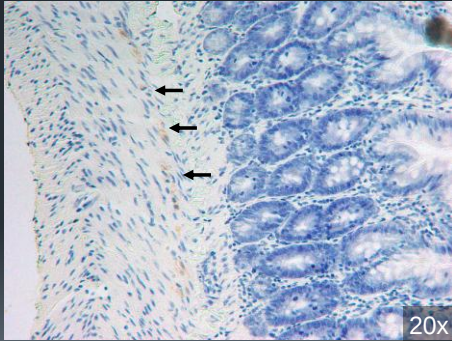
Jee, et al. World J Gastroenterol, 2010

Ileal ICC in Controls



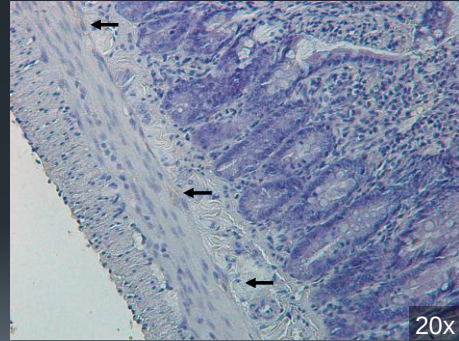
Jee, et al. World J Gastroenterol, 2010

Ileal ICC in C+/SIBO-



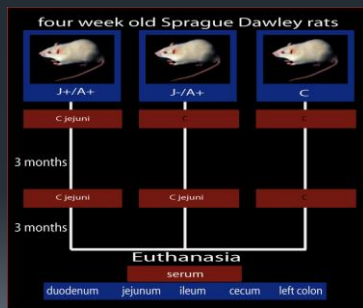
Jee, et al. World J Gastroenterol, 2010

Ileal ICC in C+/SIBO+



Jee, et al. World J Gastroenterol, 2010

Single vs Double Infection



Double Exposure: Double SIBO

